REMARKS

Status of the Claims

Claims 2, 7-26, 29-34, 36, 38-39, 44-56, 59-60, and 105-124 are currently pending in the application.

Claims 2, 29, 59 and 105 have been amended by entry of this amendment.

Claims 2, 7-26, 29-34, 36, 38-39, 44-56, 59-60, and 105-124 remain under consideration with entry of this amendment.

Summary

Claims 2, 7-26, 29-34, 36, 38-39, 44-56, 59-60, and 105-124 are pending in the application and were examined in the Office Action dated 24 April 2008. Applicants note with appreciation that the rejection of claims 2, 7-26, 29-34, 36, 38-39, 44-56, 59-60 and 105-124 under 35 U.S.C. §112, second paragraph, has been withdrawn by the Office. However, the following claim rejections have been maintained: **(a)** claims 2, 7-23, 29-34, 36, 38-39, 44-45, 47-56, 59-60 and 105-124 remain rejected under 35 U.S.C. §103(a) as unpatentable over International Publication No. WO 02/38185 to Dunn et al. ("Dunn"); **(b)** claims 24-26, 46, 55 and 56 remain rejected under 35 U.S.C. §103(a) as unpatentable over Dunn in view of International Publication No. WO 00/74650 to Brodbeck et al. ("Brodbeck1"); and **(c)** claims 122-124 remain rejected under 35 U.S.C. §103(a) as unpatentable over Dunn in view of U.S. Patent No. 6,130,200 to Brodbeck et al. ("Brodbeck2"). Applicants respectfully traverse all pending claim rejections for the following reasons.

Overview of the Amendments

Applicants, by way of this Response, have amended claims 2, 29, 59 and 105 in order to recite the invention with greater particularity. More specifically, each base claim has been amended to recite the gel structure of the recited depot compositions both prior and subsequent to administration to an implant site (tissue). Support for these

amendments can be found throughout the specification as originally filed, in particular at Paragraph [000107]. Accordingly, no new matter has been added by way of the amendments to claims 2, 29, 59 and 105, and the entry thereof is respectfully requested.

The Rejections under 35 U.S.C. §103(a)

Claims 2, 7-23, 29-34, 36, 38-39, 44-45, 47-56, 59-60 and 105-124 stand rejected under 35 U.S.C. §103(a) as obvious over Dunn. In particular, the Office asserts that Dunn teaches applicants' recited gel compositions, where the Office expressly references Dunn at page 7, lines 19-30 and Example 5, in support for the assertion that Dunn "teaches the composition is administered as a solution but forms a gel after injection." Office Action at page 2. Applicants respectfully traverse the rejection.

The Office bears the burden of establishing a *prima facie* case of obviousness under 35 U.S.C. § 103(a). *In re Fine*, 837 F.2d 1071, 1074 (Fed. Cir. 1988). According to the Federal Circuit, "the burden falls on the patent challenger to show by clear and convincing evidence that a person of ordinary skill in the art would have had reason to attempt to make the composition or device, or carry out the claimed process, and would have had a reasonable expectation of success in doing so." *Pharmastem Therapeutics, Inc. v. Viacell, Inc.*, 491 F.3d 1342, 1360 (Fed. Cir. 2007).

With regard to the Dunn compositions, it is clear that they are initially provided as a flowable composition that can be injected into tissue to form an implant "in situ", wherein the implant that is created is a "solid implant." Dunn discloses this clearly, repeatedly and emphatically in the first paragraph of their Summary of Invention (page 3, lines 14-31), where the phrase "the solid implant of the present invention occurs over and over at lines 21, 24, 27 and 30. Dunn clarifies the relationship between the initial "flowable composition" that "provides for the biodegradable implant formed *in situ*" and the resulting solid implant at page 7, lines 6-17, where they state "the biodegradable implant is formed from the steps of injecting a [flowable] composition within the body of the patient and allowing the biocompatable organic solvent to dissipate to produce a solid biodegradable implant". Dunn, page 7, lines 7-10. At page 7 of Dunn, in the paragraph found at lines 18-30 (this is the portion of the Dunn reference that the Office has

referenced to support its rejection) the idea of allowing the biocompatable solvent "to dissipate to produce a solid biodegradable implant is found at lines 21-22, and the solid implant is again described at line 26. In fact, the necessity of forming a solid implant is found throughout the Dunn specification, see e.g., page 8, lines 16, 17 18 and 20; page 9, lines 2, 8, 11-12 and 14; page 10, line 13; page 11, lines 1, and 30; page 14, lines 30-31; page 15, lines 25-27; and page 19, lines 1-4. In Example 5 (this is the second portion of the Dunn specification that the Office has referenced to support its rejection), Dunn states "[a]fter mixing to provide a uniform suspension, the contents are transferred to the syringe ... for injection into tissue where the polymer formulation solidified to form a solid depot for sustained delivery of the drug at the site of injection." Dunn, page 22, lines 17-21. Furthermore, at page 19, Dunn teaches the benefit for forming such solid structures (see lines 5-7, where they state "the release ... from these solid implants will follow the same general rules for release of a drug from a monolithic polymeric device.")

Dunn teaches two ways in which one may ensure that their solid implants can be formed. First, Dunn teaches that the selected solvent (used to produce the flowable initial composition) must be at least miscible to dispersible in aqueous medium or body fluid able to effectively dissolve the thermoplastic polyester. Dunn, page 14, lines 1-10. Suitable organic solvents for use in the Dunn systems can be found by reference to 19 granted US patents (20 patents are cited in Dunn's list on page 14, at lines 7-9; however, one document (US 5,763,152) relates to silver halide photographic light-sensitive materials, and is thus thought to be a typographical error). A review of the remaining 19 cited patents reveals that each document includes Richard L. Dunn as a named inventor, each is assigned to Atrix Laboratories, and each document relates to *in situ* forming polymeric implants (except for one which relates to non-polymeric systems (US 5,888,533) -- therefore the cited documents are directly relevant to the understanding the Dunn reference that has been cited in the instant application, since they relate to the exact same depot technology. The patents that have been expressly referenced by Dunn teach suitable solvents for Dunn's polymer depots are as follows: "the solvent [should be or is] water miscible so that it will diffuse quickly into the body fluids and allow water to permeate into the polymer solution and cause it to coagulate or solidify" see US Pat Nos.

4,938,763; 5,278,201; 5,702,716; 5,707,647; 5,717,030; 5,733,950; 5,739,176; 5,945,115; and 5,990,194; or suitable solvents are "miscible with the polymer component and water, and capable of diffusing into tissue fluids surrounding the implant site [and] the degree of polarity of the solvent should be effective to provide at least about 10% solubility in water" and further that "a mixture of solvents can be used to increase the coagulation rate of polymers which exhibit slow coagulation or setting rate" see US Patent Nos. 5,324,519; 5,487,897; 5,599,552; 5,632,727; 5,725,491; 5,744,153; 5,759,563; 5,780,044; and 5,792,469.

The second way that Dunn teaches to ensure that a solid implant is formed is as follows: "the higher molecular weight polymers will normally tend to coagulate or solidify faster than the very low-molecular weight polymers." Dunn, page 15, lines 25-27. Thus, Dunn teaches that the higher molecular weight polymers will favor the required formation of a solid implant system after implantation.

Accordingly, the scope and content of the Dunn reference, when considered fairly and as a whole, teaches injectable depot compositions that contain a solvent selected to quickly leave the injection site to enable the formation of a solid implant. The Dunn solvents leave the injection site quickly to "allow water to permeate into the polymer solution and cause it to coagulate or solidify." Furthermore, the scope and content of the Dunn reference teach selection of solvents that have an affinity (water–solubility, –miscibility, or –diffusibility) for leaving the polymer depot (again to facilitate rapid or quick setting of the solid implant system), and furthermore, if solvents not having this feature are used, Dunn teaches how additional solvents can be mixed into the composition in order to quicken setting of the solid implant. Dunn teaches selection of higher molecular weight polymers to facilitate faster solidification of the solid implant. Finally, Dunn teaches that the solid form implants are beneficial since release from such solid implants "will follow the same general rules for release of a drug from a monolithic polymeric device."

The difference between Dunn and applicants' recited gel compositions is manifest. Applicants teach depot gel compositions that retain their gel-like consistency after implantation (the injectable gel compositions form gel implants). A gel is not a

solid. Applicants teach selection of solvents to "substantially restrict uptake of water by the implant and which are characterized as immiscible with water (having a water solubility less than 7%, preferably less that 5%, more preferably less than 3% and even more preferably less than 1% or less." Applicants' specification, paragraph [00087]. Applicants teach selection of low molecular weight polymers. The combination of these low molecular weight polymers with the water immiscible solvents allow applicants' recited gel depot compositions to avoid the formation of a solid implant, rather applicants gel composition are thought to retain their gel structure after implantation, and thus according to Dunn they would not be expected to mimic release characteristics of a monolithic polymeric device.

Accordingly, when applicants' recited gel compositions and Dunn's solid depot compositions are fairly considered as a whole, it is clear that the systems are manifestly different. Dunn teaches selection criteria for both the solvent and the polymer that would render applicants' compositions non-functional. Conversely, applicants teach selection criteria for both the solvent and the polymer that would render Dunn's implant compositions non-functional. In other words, the Office has failed to establish a *prima facie* case of obviousness under 35 U.S.C. § 103(a), since it has not shown by clear and convincing evidence that a person of ordinary skill in the art would have had reason to ignore every component selection teaching provided by Dunn to make solid implants compositions and instead attempt to make applicants' recited gel depot compositions, and that the skilled person would have had a reasonable expectation of success in doing so. Accordingly, the rejection of claims 2, 7-23, 29-34, 36, 38-39, 44-45, 47-56, 59-60 and 105-124 under 35 U.S.C. §103(a) as obvious over Dunn is improper. Reconsideration and withdrawal of the rejection is thus earnestly solicited.

Claims 24-26, 46, 55 and 56 stand rejected under 35 U.S.C. §103(a) as obvious over Dunn in further view of Brodbeck1 for reasons of record. Applicants respectfully traverse the rejection.

In particular, applicants have established herein above that the primary reference to Dunn relates to an entirely different sort of implant technology. Dunn teaches solvent selection to facilitate rapid removal of the solvent from the polymer system to provide

their solid implant structures. Dunn's solvent is further selected to attract water into the polymer depot to permeate the polymer system and cause it to coagulate or solidify. Dunn teaches polymers with higher molecular weight can be selected to decrease time for solidification. Furthermore, if solvents with lower water solubility are used, Dunn teaches that they should be combined with a more water-soluble solvent, again to hasten solidification. Brodbeck1 teaches gel systems. A gel is not a solid. Accordingly, the Office's assertion that Dunn and Brodbeck1 would be combined by the skilled person in order to arrive at applicants' recited gel compositions simply does not carry persuasive weight. This is because Dunn expressly teaches away from applicants' solvent and polymer selection criteria, and changing Dunn in the manner that the Office has suggested would render Dunn's solid implant systems unsatisfactory for their intended purpose. It is improper to combine references where the references themselves teach away from their combination. *In re Grasselli*, 218 USPQ 769, 779 (Fed. Cir. 1983).

For all of these reasons, then, the rejection of claims 24-26, 46, 55 and 56 under 35 U.S.C. §103(a) as unpatentable over the combination of Dunn and Brodbeck1 is improper. Reconsideration and withdrawal of the rejection is thus earnestly solicited.

Claims 122-124 stand rejected under 35 U.S.C. §103(a) as obvious over Dunn in further view of Brodbeck2 for reasons of record. Applicants respectfully traverse the rejection.

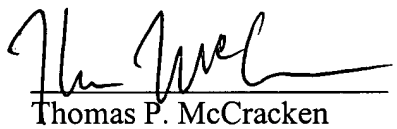
Here again, the Office's proposed combination of Dunn and Brodbeck2 is improper since Dunn expressly teaches away from applicants' solvent and polymer selection criteria, and changing Dunn in the manner that the Office has suggested would render Dunn's solid implant systems unsatisfactory for their intended purpose. *In re Grasselli*, 218 USPQ 769, 779 (Fed. Cir. 1983).

For all of these reasons, then, the rejection of claims 122-124 under 35 U.S.C. §103(a) as unpatentable over the combination of Dunn and Brodbeck2 is improper. Reconsideration and withdrawal of the rejection is thus earnestly solicited.

CONCLUSION

Applicants submit that the pending claims define an invention that is both novel and nonobvious over the cited art, and thus all claims are in condition for allowance. Acknowledgement of this by the Office in the form of an early allowance is thus respectfully requested. In addition, if the Examiner contemplates other action, or if a telephone conference would expedite allowance of the claims, applicants invite the Examiner to contact the undersigned at (408) 777-4915.

Respectfully submitted,



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